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10/519,259	02/14/2006	Michael Schutz	DEBE:046US	3637

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,259	SCHUTZ ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group II, claims 4-10, in the reply filed on February 28, 2007 is acknowledged. The traversal is on the ground(s) that the reference (Nesper et al. 2000) does not teach the special technical feature. Nesper et al. (2000) teach the use of whole bacteriophage, not isolated bacteriophage tail proteins, the latter now being recited in all the pending claims. The restriction requirement of the previous Office action is hereby withdrawn.

Claims 1-18 are pending and currently under examination.

Priority: The benefit date is June 24, 2002 for the purpose of prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the genus of bacteriophage tail proteins is discussed in the specification, there is no evidence that any representative species of such a large and varied genus was in the possession of the inventors at the time of filing. To satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the

identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. The specification does not disclose any representative species of bacteriophage tail proteins, with or without identifying characteristics. Only one species is provided, p12 protein of phage T4, which is insufficient to define the genus. Therefore, the instant claims, as written, fails to satisfy the written description requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1(a) recites incubating a sample with an isolated bacteriophage tail protein. However, claim 2(a') recites separating bacteriophage tail protein-endotoxin complexes from the sample. Claim 1(b) recites detecting endotoxin bonded to bacteriophage tail proteins. The instant claims are indefinite because it is unclear if the sample is incubated with a single bacteriophage tail protein or multiple tail proteins. For examination purposes, it is assumed that said protein(s) is more than one.

Claim 3 is included in this rejection because it is dependent on claim 1 and fails to cure the defect.

Claim 4 has the opposite problem of claims 1 and 2. Claim 4(a) recites incubating a sample with isolated bacteriophage tail proteins but claim 4(b) recites separating a singular tail protein-endotoxin complex from the sample. Therefore, the claim is indefinite.

Claims 4, 7, 10 recite a permanent carrier. The claims are indefinite because neither the claims nor the specification have explicitly defined what a "permanent carrier" is.

Claim 6 recites centrifugations materials. The claim is indefinite because it is unclear what centrifugation materials are.

Claim 12 recites the tag comprises an amino acid sequence according to SEQ ID NOS. 5, 6, or 7. The claim is dependent on claim 11, which recites a Strep-tag or a His-tag. It is unclear which "tag" the SEQ ID NOS. are referring to, i.e. Strep-tag or His-tag.

Claim 13 recites the limitation "p12 protein of the phage T4" in the claim. There is insufficient antecedent basis for this limitation in the claim and the parent claim.

Claim 14 recites the limitation "Ca^{2+} concentration...and the Mg^{2+} concentration" in the claim. There is insufficient antecedent basis for this limitation in the claim and the parent claim.

Claim 15 recites marked endotoxin being displaced from the bond with the bacteriophage tail protein and the marked endotoxin being subsequently deleted. The claim is confusing because it is unclear what the marked endotoxin is referring to and how is it marked.

Claims 5, 8-9, 11, 16-18 are included in this rejection because they are dependent on the above claims and fail to cure the defect.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 7, 10-11, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (1999 Virus Research 60: 95-99). Suzuki et al. teach the specific interaction of fused H protein of bacteriophage ϕX174 with receptor lipopolysaccharides (LPS). Various concentrations of HisH (histidine-tagged H protein) were adsorbed onto 96 flat-bottom wells, rinsed, and incubated with a sample of biotinylated LPS (p. 97 col. 2; claims 1, 4, 10, 7, 11). The wells were washed to remove unbound LPS, and then added with streptavidin-peroxidase complex (p. 98 col. 1; claims 2). The bound biotinylated LPSs were detected at absorbance of 490 nm (p. 98 Fig. 3; claims 2-4, 15). In Figure 3, Suzuki et al. teach the dose-dependent binding of biotinylated LPS from *E. coli* to HisH (histidine-tagged H protein) (p. 98; claims 1, 3, 11, 15).

Claims 1-3, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Baxa et al. (1996 Biophysical Journal 71: 2040-2048). Baxa et al. teach bacteriophage p22 tail protein binds to the O-antigen structure in *Salmonella* lipopolysaccharide (LPS) (p. 2040). Soluble tailspikes were studied using octa- and dodecasaccharides comprising two and three O-antigen

repeats of *Salmonella* LPSs (p. 2040). Baxa et al. teach LPS fragments were chemically labeled at their reducing ends with fluorophore Amc (p. 2041 col. 2; claim 15). Baxa et al. teach p22 tailspike proteins were incubated with labeled LPS fragments, wherein aliquots of bound bacteriophage tail protein-LPS were removed, and analyzed by reverse-phase HPLC on an ODS column at a flow rate of 1 mL/min. (p. 2042 col. 1; claims 1-2). The Amc label was detected at an excitation wavelength of 360 nm and an emission wavelength of 450 nm (p. 2042 col. 1; claim 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-8, 10, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller (US 7087376). Miller teaches a method for the detection of bacteria comprising (a) immobilizing at least T4 p12 protein to a support; (b) incubating the support coupled to the T4 p12 with a sample; (c) detecting bacteria bound to the T4 p12 protein (col. 9-10 lines 32-5). The bound bacteria were separated from the unbound sample by washing steps and detected spectrometrically at 405 nm (col. 9 lines 20-31). The support can be selected from filter material, glass, PMMA, polycarbonate (col. 10 lines 29-33). Miller further teaches the T4 p12 protein can be bound to said support through a polypeptide immobilized to the support, i.e. antibody, lectin, receptor, or anticalin (col. 10 lines 21-23). The bacteriophage tail proteins are

immobilized on the support by covalent bonding (col. 9 lines 1-15). Miller discloses phages bind to bacteria through protein-protein, protein-carbohydrate, or protein-lipid interactions, and that the detection method can be used to detect bacteria that are relevant in for the food industry, medicine, e.g. *E. coli*, salmonella. The detection can be performed by immunologic detection and/or colorimetric detection (col. 10 lines 10-13). Miller does not explicitly teach detecting endotoxin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Miller for detecting endotoxin by incubating a sample with isolated bacteriophage tail proteins (T4 p12) which are covalently bound to a support (claim 1a, 4a, 10), separating the bound endotoxin-bacteriophage tail protein complex from the sample (claim 2a[1], 4b), and detecting the bound endotoxin by spectroscopic means (claim 3, 15). It would also have been obvious to substitute the different types of carriers, i.e. glass, filtration material, and use a polypeptide, i.e. antibody, lectin, to bind the T4 p12 tail protein to the support because Miller discloses these modifications can be used in the detection method (claims 6-8). One of ordinary skill would be motivated to use the method of Miller to detect endotoxin and expect to be successful because Miller discloses preferred bacteria that can be used in his method include gram-negative bacteria such as *E. coli* and salmonella, which comprises endotoxin in their outer membranes.

Claims 4-6, 7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baxa et al. (1996 Biophysical Journal 71: 2040-2048) in view of Sun et al. (2000 J Industrial

Microbiology & Biotechnology 25: 273-275; IDS). The teachings of Baxa et al. are outlined above. Baxa et al. do not teach immobilization of the phage tail proteins on a carrier.

Sun et al. disclose the efficiency of a phage-based biosorbent consisting of a *Salmonella*-based phage immobilized on a polystyrene membrane used to separate *Salmonella* from food materials was poor (p. 273 col. 1). Sun et al. teach the construction of a bacteriophage-based biosorbent comprising the biotinylation of phage SJ2, coating the biotinylated phage onto streptavidin-labeled magnetic beads, and incubating the biosorbent with bioluminescent *Salmonella* (p. 274 col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to remove endotoxin by modifying the method of Baxa et al. such that LPS is incubated with phage tail proteins immobilized onto the streptavidin-labeled carrier of Sun et al. before being subject to the column chromatography analysis of Baxa et al. (claims 4-6, 7, 9). One of ordinary skill in the art would be motivated to immobilize phage tail proteins onto a carrier, i.e. magnetic beads, sedimentation materials, through a streptavidin-biotin interaction because Sun et al. teach the efficient capture of *Samonella* was observed by this bacteriophage-based biosorbent. One of ordinary skill would also recognize that *Salmonella* comprises endotoxin on its outer membrane and that whole bacteriophage also inherently comprises tail protein; therefore, the biosorbent of Sun et al. can be successfully used in the method of Baxa et al.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and

useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claims 11-13 be found allowable, claims 16-18 will be objected to under 37 CFR 1.75 as being a complete duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 13-16, 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 7087376 ('376). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '376 claims are both drawn to a method of detecting and/or removing endotoxin comprising incubating a sample with bacteriophage tail protein, separating the tail protein-endotoxin complex, and detecting the endotoxin. While the '376 claims do not explicitly state the detection of endotoxin (currently recited in the instant claims), they are not patentably distinct from the instant invention because it is known in the art that the preferred bacteria of the '376 claims inherently comprise endotoxin in their outer membrane, e.g. *E. coli*, salmonella ('376 patent col. 3 line 56).

Claims 1-11, 13-16, 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-28 of copending Application No. 10583415 ('415). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '415 claims are both drawn to a method for detecting endotoxin comprising the steps of incubating a sample with bacteriophage tail proteins immobilized on a surface, and removing and/or detecting the phage tail protein-endotoxin complex by spectroscopic means.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-11, 13-16, 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-11, 16, 17-27 of copending Application No. 10470797 ('797). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '797 claims are both drawn to a method of detecting and/or removing endotoxin comprising incubating a sample with bacteriophage tail protein, separating the tail protein-endotoxin complex, and detecting the endotoxin. While the '797 claims do not explicitly state the detection of endotoxin (currently recited in the instant claims), they are not patentably distinct from the instant invention because it is known in the art that the bacteria detected in the '797 claims inherently comprise endotoxin in their outer membrane, e.g. *E. coli*, salmonella.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-11, 13-16, 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-23 of copending Application No. 11445451 ('451). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '451 claims are both drawn to a method of detecting and/or removing endotoxin comprising incubating a sample with bacteriophage tail protein, separating the tail protein-endotoxin complex, and detecting the endotoxin. While the '451 claims do not explicitly state the detection of endotoxin (currently recited in the instant claims), they are not patentably distinct from the instant invention because it

is known in the art that the bacteria detected in the '451 claims inherently comprise endotoxin in their outer membrane, e.g. *E. coli*, salmonella.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10482235 ('235). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '235 claims are both drawn to a method of detecting and/or removing endotoxin comprising incubating a sample with bacteriophage tail protein, separating the tail protein-endotoxin complex, and detecting the endotoxin. While the '235 claims do not explicitly state the detection of endotoxin (currently recited in the instant claims), they are not patentably distinct from the instant invention because it is known in the art that the bacteria detected in the '235 claims inherently comprise endotoxin in their outer membrane, e.g. *E. coli*, salmonella.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

April 25, 2007

M. Monshi

MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER